

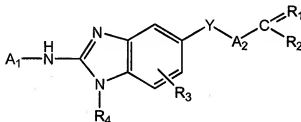
## AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

### Listing of claims:

1-74. (Canceled)

75. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated cancer disorder selected from the group consisting of melanoma, breast cancer, prostate cancer, lung cancer, pancreatic cancer, thyroid cancer, bladder cancer, colon cancer, liver cancer, myeloid leukemia, and villous colon adenoma, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (II) effective to inhibit Raf kinase activity in the human or animal subject:



(II)

wherein Y is O;

A<sub>1</sub> is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, ~~polycyclic~~ aryl, ~~polycyclic~~ arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

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A<sub>2</sub> is ~~substituted or~~ unsubstituted heteroaryl;

R<sub>1</sub> is O or H, and R<sub>2</sub> is NR<sub>5</sub>R<sub>6</sub> or hydroxyl; or R<sub>1</sub> is taken together with R<sub>2</sub> to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R<sub>3</sub> is hydrogen, halogen, loweralkyl, or loweralkoxy; and

R<sub>4</sub> is ~~hydrogen, hydroxyl, alkylamino, dialkylamino or~~ alkyl; [[and]]

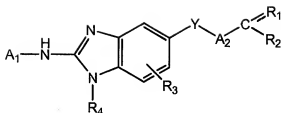
R<sub>5</sub> and R<sub>6</sub> are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxyalkylheterocyclo, and heteroarylalkyl; or R<sub>5</sub> and R<sub>6</sub> are taken together to form substituted or unsubstituted heterocyclo or heteroaryl;

or a pharmaceutically acceptable salt thereof.

76. (Previously presented) The method of claim 75 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

77. (Canceled)

78. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated hormone dependent cancer disorder selected from the group consisting of breast cancer and prostate cancer, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (II) effective to inhibit Raf kinase activity in the human or animal subject:



(II)

wherein Y is O;

~~A<sub>1</sub> is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;~~

~~A<sub>2</sub> is substituted or unsubstituted heteroaryl;~~

~~R<sub>1</sub> is O or H, and R<sub>2</sub> is NR<sub>5</sub>R<sub>6</sub> or hydroxyl; or R<sub>1</sub> is taken together with R<sub>2</sub> to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;~~

~~R<sub>3</sub> is hydrogen, halogen, loweralkyl, or loweralkoxy; and~~

~~R<sub>4</sub> is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl; [[and]]~~

~~R<sub>5</sub> and R<sub>6</sub> are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxyalkylheterocyclo, and heteroarylalkyl; or R<sub>5</sub> and R<sub>6</sub> are taken together to form substituted or unsubstituted heterocyclo or heteroaryl;~~

~~or a pharmaceutically acceptable salt thereof.~~

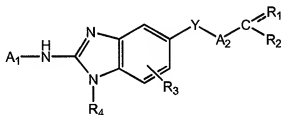
79. (Canceled)

80. (Previously presented) The method of claim 78 which further comprises administering to the human or animal subject at least one additional agent for the treatment of

cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

81. (Canceled)

82. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated hematological cancer disorder, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (II) effective to inhibit Raf kinase activity in the human or animal subject:



(II)

wherein Y is O;

A<sub>1</sub> is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A<sub>2</sub> is substituted or unsubstituted heteroaryl;

R<sub>1</sub> is O or H, and R<sub>2</sub> is NR<sub>5</sub>R<sub>6</sub> or hydroxyl; or R<sub>1</sub> is taken together with R<sub>2</sub> to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R<sub>3</sub> is hydrogen, halogen, loweralkyl, or loweralkoxy; and

~~R<sub>4</sub> is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl; [[and]]~~

~~R<sub>5</sub> and R<sub>6</sub> are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxyalkylheterocyclo, and heteroarylalkyl; or R<sub>5</sub> and R<sub>6</sub> are taken together to form substituted or unsubstituted heterocyclo or heteroaryl;~~  
or a pharmaceutically acceptable salt thereof.

83. (Previously presented) The method of claim 82 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

84-87. (Canceled)

88. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R<sub>4</sub> in formula (II) is ~~hydrogen or C<sub>1-6</sub> alkyl~~.

89. (Previously presented) The method of claim 88, wherein R<sub>4</sub> in formula (II) is methyl.

90. (Canceled)

91. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A<sub>1</sub> in formula (II) is ~~a substituted or unsubstituted C<sub>3-14</sub> aryl~~ carbocyclic aryl group.

92. (Currently amended) The method of claim ~~[[91]]~~ 75, wherein A<sub>1</sub> in formula (II) is selected from the group consisting of substituted ~~or unsubstituted~~ phenyl, pyridyl, pyrimidinyl,

phenylalkyl, pyridylalkyl, pyrimidinylalkyl, heterocyclylcarbonylphenyl, heterocyclylphenyl, heterocyclylalkylphenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkylbenzoate, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, thiophene, thiophenyl, thiophene-2-carboxylate, alkylthiophenyl, trifluoromethylphenyl, — acetylphenyl, — sulfamoylphenyl, — biphenyl, — cyclohexylphenyl, phenyloxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl, alkylfluorophenyl, trifluoromethylchlorophenyl, — trifluoromethylbromophenyl, indenyl, 2,3-dihydroinderyl, tetralinyl, — trifluorophenyl, — (trifluoromethyl)thiophenyl, — alkoxybiphenyl, — morpholinyl, N-piperazinyl, — N-morpholinylalkyl, — piperazinylalkyl, — cyclohexylalkyl, — indolyl, 2,3-dihydroindolyl, — 1-acetyl-2,3-dihydroindolyl, — cycloheptyl, — bicyclo[2.2.1]hept-2-yl, hydroxyphenyl, — hydroxyalkylphenyl, — pyrrolidinyl, — pyrrolidin-1-yl, — pyrrolidin-1-ylalkyl, 4-amino(imino)methylphenyl, isoxazolyl, indazolyl, adamantyl, bicyclohexyl, quinolindinyl, imidazolyl, benzimidazolyl, imidazolylphenyl, phenylimidazolyl, phthalimide, naphthyl, benzophenone, aniliny, anisoly, quinolinyl, quinolinonyl, phenylsulfonyl, phenylalkylsulfonyl, 9H-fluoren-1-yl, piperidin-1-yl, piperidin-1-ylalkyl, cyclopropyl, cyclopropylalkyl, pyrimidin-5-ylphenyl, quinolidinylphenyl, or furanyl, furanylphenyl, N-methylpiperidin-4-yl, pyrrolidin-4-ylpyridinyl, — 4-diazepan-1-yl, — hydroxypyrrolidin-1-yl, — dialkylaminopyrrolidin-1-yl, 1,4'-bipiperidin-1'-yl, and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

93. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A<sub>1</sub> in formula (II) is selected from the group consisting of substituted or unsubstituted phenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenyloxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl,

alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, hydroxyphenyl, hydroxyalkylphenyl, 4-amino(imino)methylphenyl and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

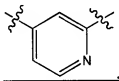
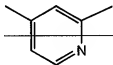
94. (Previously presented) The method of claim 93, wherein A<sub>1</sub> in formula (II) is 4-bromophenyl.

95. (Previously presented) The method of claim 93, wherein A<sub>1</sub> in formula (II) is trifluoromethylchlorophenyl.

96. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A<sub>2</sub> in formula (II) is selected from the group consisting of ~~substituted or unsubstituted phenyl~~, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinolinyl, purinyl, ~~naphthyl~~, benzothiazolyl, benzopyridyl and benzoimidazolyl.

97. (Currently amended) The method of claim 96, wherein A<sub>2</sub> in formula (II) is unsubstituted pyridyl.

98. (Currently amended) The method of claim 96, wherein A<sub>2</sub> in formula (II) is



99. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R<sub>1</sub> is taken together with R<sub>2</sub> in formula (II) to form a substituted ~~or unsubstituted~~ C<sub>3-8</sub> ~~heterocycloalkyl or C<sub>3-14</sub> heteroaryl group, wherein the C<sub>3-14</sub> heteroaryl group contains only carbon and nitrogen atoms as ring atoms.~~

100. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R<sub>1</sub> is taken together with R<sub>2</sub> in formula (II) to form a group selected from substituted ~~or unsubstituted~~ phenyl, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinoliny, purinyl, ~~naphthyl~~, benzothiazolyl, benzopyridyl and benzoimidazolyl.

101. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R<sub>1</sub> is taken together with R<sub>2</sub> in formula (II) to form a substituted ~~or unsubstituted~~ imidazolyl group.

102. (Previously presented) The method of claim 100, wherein the imidazolyl group is substituted with a halo C<sub>1-6</sub> alkyl group.

103. (Previously presented) The method of claim 100, wherein the imidazolyl group is substituted with a trifluoromethyl group.

104-107. (Canceled)

108. (Previously presented) The method of claim 75, wherein the cancer is melanoma.

109. (Previously presented) The method of claim 75, wherein the cancer is a carcinoma of the lungs, pancreas, thyroid, bladder or colon.



110. (Previously presented) The method of claim 75, wherein the cancer is myeloid leukemia.

111. (Previously presented) The method of claim 75, wherein the cancer is villous colon adenoma.

112. (Previously presented) The method of claim 82 wherein the hematological cancer disorder is chronic myelogenous leukemia.

113. (New) The method of claim 75, wherein A<sub>1</sub> in formula (II) is selected from the group consisting of phenylalkyl, pyridylalkyl, pyrimidinylalkyl, heterocyclylcarbonylphenyl, heterocyclylphenyl, heterocyclylalkylphenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkylbenzoate, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, thiophene-2-carboxylate, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenyloxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl, alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, 2,3-dihydroindenyl, tetralinyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, indolyl, 2,3-dihydroindolyl, 1-acetyl-2,3-dihydroindolyl, hydroxyphenyl, hydroxyalkylphenyl, 4-amino(imino)methylphenyl, imidazolylphenyl, phenylimidazolyl, pthalamido, benzophenone, aniliny, anisolyl, quinolinonyl, phenylsulfonyl, phenylalkylsulfonyl, pyrimidin-5-ylphenyl, quinolidinylphenyl, furanylphenyl, pyrrolidin-4-ylpyridinyl, and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

114. (New) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein the variables in formula (II) are as follows:

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A<sub>1</sub> is a substituted carbocyclic aryl group;

A<sub>2</sub> is unsubstituted pyridyl;

R<sub>1</sub> is taken together with R<sub>2</sub> to form a substituted C<sub>3-14</sub> heteroaryl group, wherein the C<sub>3-14</sub> heteroaryl group contains only carbon and nitrogen atoms as ring atoms; and

R<sub>4</sub> is C<sub>1-6</sub> alkyl;

or a pharmaceutically acceptable salt thereof.

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